



Europäisches Patentamt  
European Patent Office  
Office européen des brevets



Publication number:

**0 555 880 A3**

(12)

## EUROPEAN PATENT APPLICATION

(21) Application number: 93102279.2

(51) Int. Cl.<sup>5</sup>: C07K 15/00, C12P 21/08,  
A61K 37/02, A61K 39/395

(22) Date of filing: 12.02.93

(30) Priority: 14.02.92 US 835799

(43) Date of publication of application:  
18.08.93 Bulletin 93/33

(84) Designated Contracting States:  
AT BE CH DE DK ES FR GB GR IE IT LI LU MC  
NL PT SE

(86) Date of deferred publication of the search report:  
11.05.94 Bulletin 94/19

(71) Applicant: Bristol-Myers Squibb Company  
345 Park Avenue  
New York, N.Y. 10154(US)  
Applicant: TRUSTEES OF DARTMOUTH  
COLLEGE  
P.O. Box 7  
Main Street  
Hanover, NH 03755(US)  
Applicant: THE GENERAL HOSPITAL  
CORPORATION

55 Fruit Street  
Boston, MA 02114(US)

(72) Inventor: Aruffo, Alejandro A.  
1012 Spruce Street  
Edmonds, WA 98020(US)  
Inventor: Ledbetter, Jeffrey A.  
306 N.W. 113th Place  
Seattle, WA 98177(US)  
Inventor: Noell, Randolph  
Freeman Hill Road  
Plainfield, NH 03781(US)  
Inventor: Stamenkovic, Ivan  
59 Babcock Street  
Brookline, MA 02146(US)

(74) Representative: Kinzebach, Werner, Dr. et al  
Patentanwälte  
Reitstötter, Kinzebach und Partner  
Sternwartstrasse 4  
Postfach 86 06 49  
D-81633 München (DE)

(54) The CD40CR receptor and ligands therefor.

(57) The present invention relates to a counter-receptor, termed CD40CR, for the CD40 B-cell antigen, and to soluble ligands for this receptor, including fusion molecules comprising at least a portion of CD40 protein. It is based, at least in part, on the discovery that a soluble CD40/immunoglobulin fusion protein was able to inhibit helper T-cell mediated B-cell activation by binding to a novel 39 kD protein receptor on helper T-cell membranes. The present invention provides for a substantially purified CD40CR receptor; for soluble ligands of CD40CR, including antibodies as well as fusion molecules comprising at least a portion of CD40 protein; and for methods of controlling B-cell activation which may be especially useful in the treatment of allergy or autoimmune disease.

EP 0 555 880 A3



European Patent  
Office

## EUROPEAN SEARCH REPORT

Application Number  
EP 93 10 2279

DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim
A	TISSUE ANTIGENS vol. 36, no. 1, July 1990, COPENHAGEN, DENMARK pages 33 - 36 E. CLARK 'CD40, a cytokine receptor in search for a ligand.' * the whole document *	1-4
P,X	IMMUNOLOGY TODAY vol. 13, no. 11, November 1992, AMSTERDAM, THE NETHERLANDS pages 431 - 433 R. NOELLE ET AL. 'CD40 and its ligand, an essential ligand-receptor pair for thymus-dependent B-cell activation.' * the whole document *	1-23
P,X	NATURE vol. 357, no. 6373, 7 May 1992, LONDON, GREAT BRITAIN pages 80 - 82 R. ARMITAGE ET AL. 'Molecular and biological characterization of a murine ligand for CD40.' * the whole document *	1-3, 5-10, 14-17
P,X	EUROPEAN JOURNAL OF IMMUNOLOGY vol. 22, no. 10, October 1992, WEINHEIM, GERMANY pages 2573 - 2578 P. LANE ET AL. 'Activated human T cells express a ligand for the human B cell-associated antigen CD40 which participates in T cell-dependent activation of B lymphocytes.' * the whole document *	1-3, 5-10, 14-17
The present search report has been drawn up for all claims		
Place of search THE HAGUE		Date of completion of the search 21 March 1994
Examiner Noel J. F		
<b>CATEGORY OF CITED DOCUMENTS</b>		
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons a : member of the same patent family, corresponding document		

EP 93 10 2279 (PCT)



European Patent  
Office

## EUROPEAN SEARCH REPORT

Application Number  
EP 93 10 2279

DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim
P,X	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA vol. 89, no. 14, 15 July 1992, WASHINGTON DC, USA pages 6550 - 6554 R. NOELLE ET AL. 'A 39-kDa protein on activated helper T cells bind CD40 and transduces the signal for cognate activation of B cells.' * the whole document *	1-3, 5-10, 14-17
P,X	EUROPEAN JOURNAL OF IMMUNOLOGY vol. 22, no. 12, December 1992, WEINHEIM, GERMANY pages 3191 - 3194 D. GRAF ET AL. 'Cloning of TRAP, a ligand for CD40 on human T cells.' * abstract *	1,3, 5-10, 14-17
The present search report has been drawn up for all claims		
Place of search THE HAGUE		Date of completion of the search 21 March 1994
		Examiner Noofj, F
<b>CATEGORY OF CITED DOCUMENTS</b>		
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		
T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons @ : member of the same patent family, corresponding document		

EPO FORM 650 (6/92) (P0402)